

A

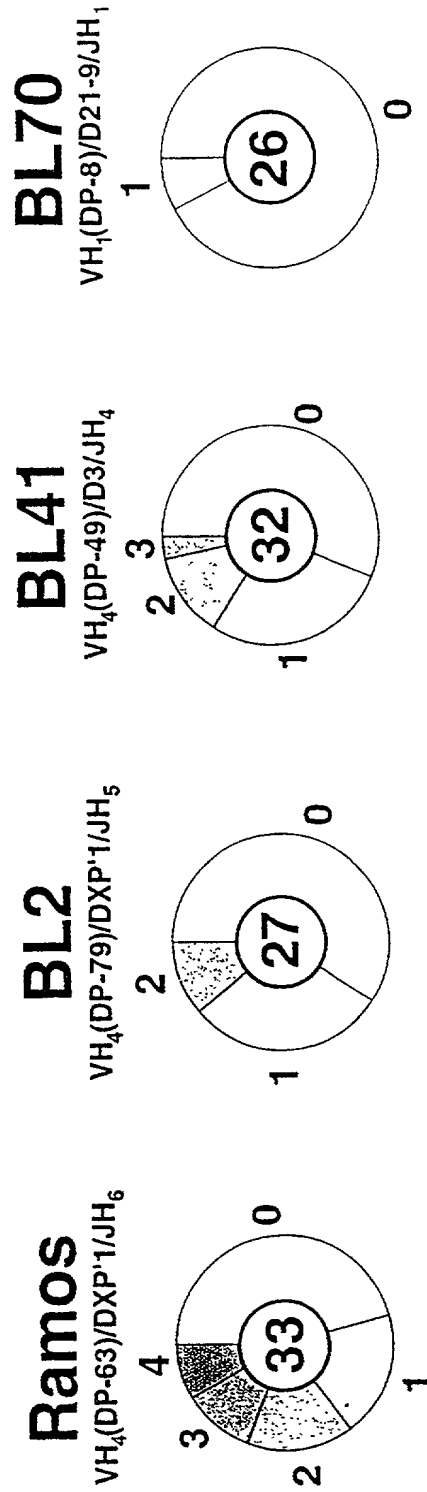


FIG. 1

B

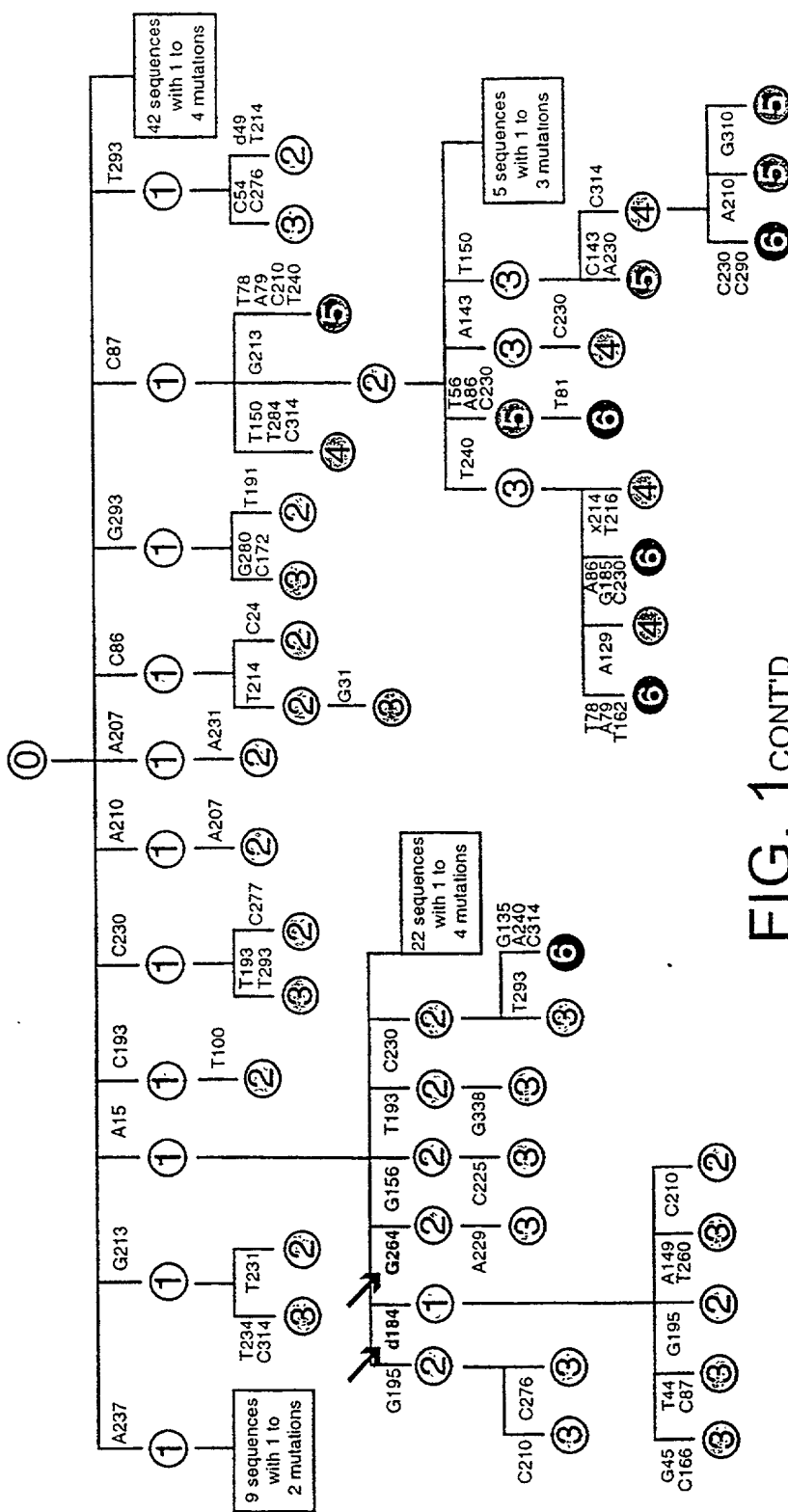
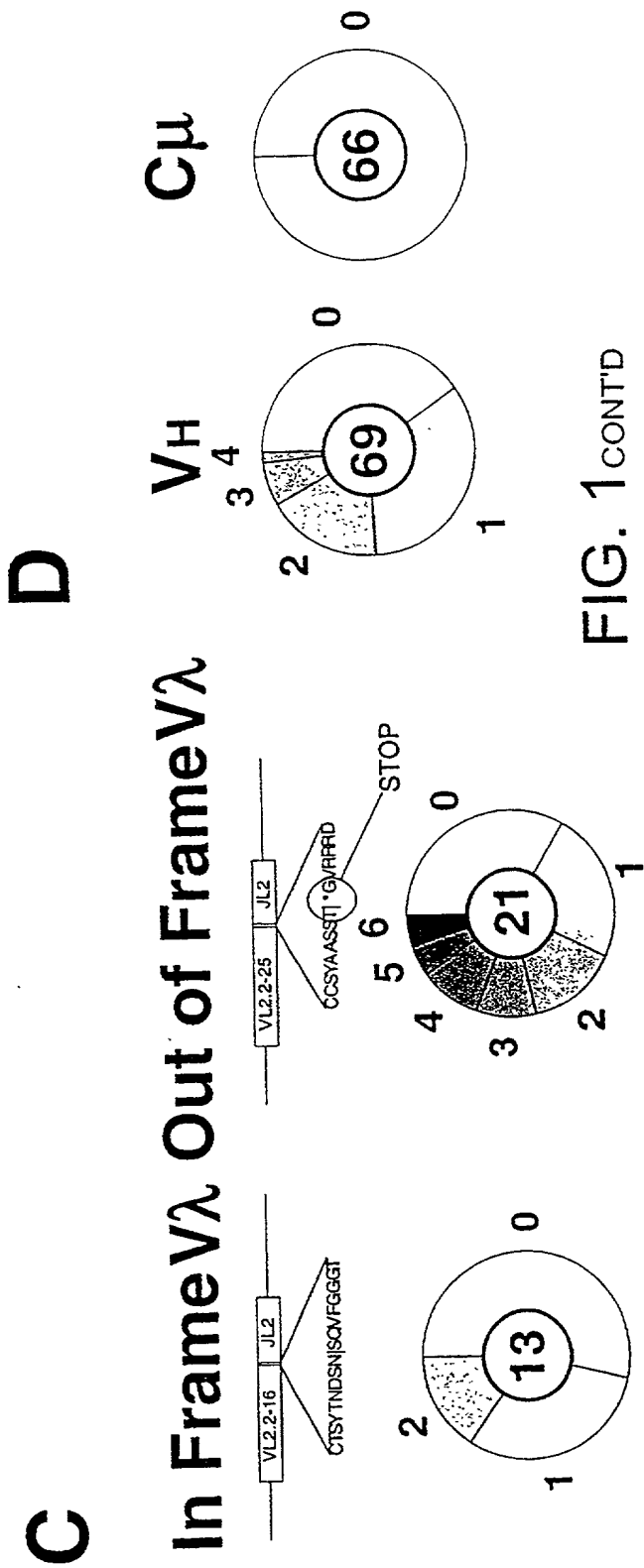
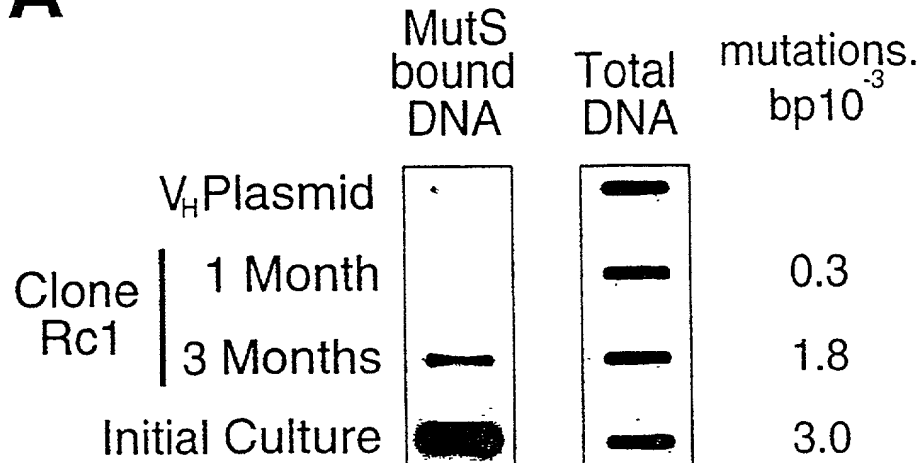
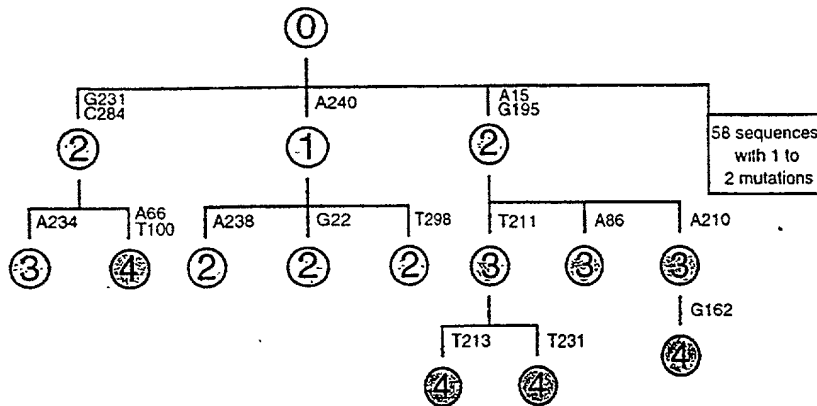
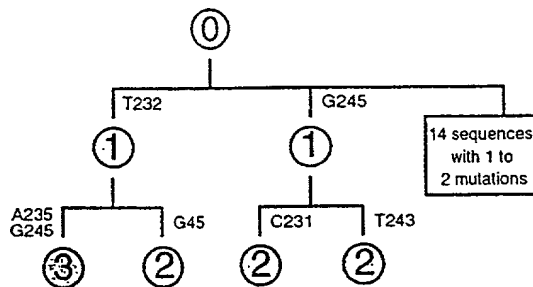
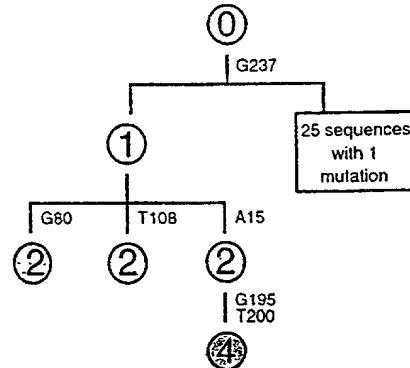


FIG. 1 CONT'D



A**B****Clone Rc13** $0.24 \times 10^{-4} \text{ mutn. bp}^{-1} \text{ div}^{-1}$ **Clone Rc14** $0.22 \times 10^{-4} \text{ mutn. bp}^{-1} \text{ div}^{-1}$ **Clone Rc1** $0.27 \times 10^{-4} \text{ mutn. bp}^{-1} \text{ div}^{-1}$ **FIG. 2**

CDR1

CDR2

82a

DXP-1

9H6 ←

FIG. 3

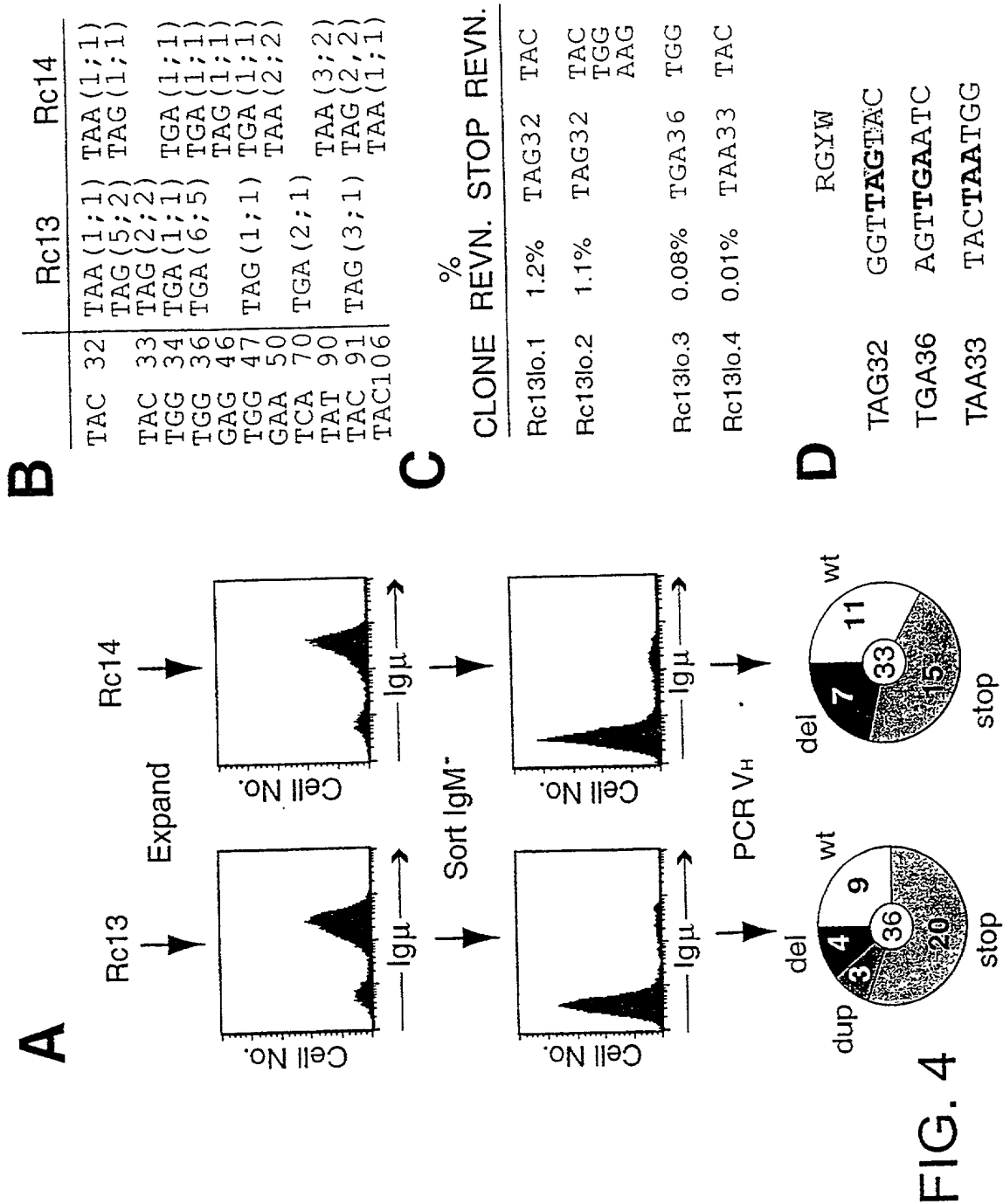


FIG. 4

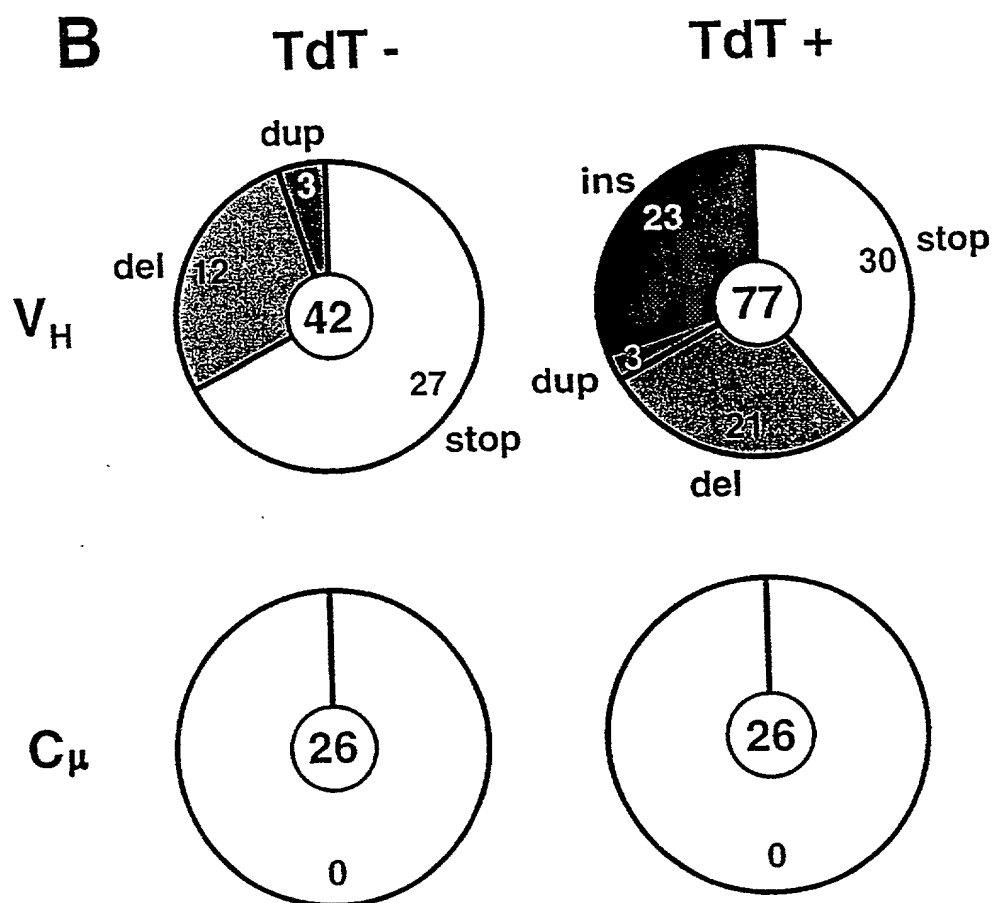
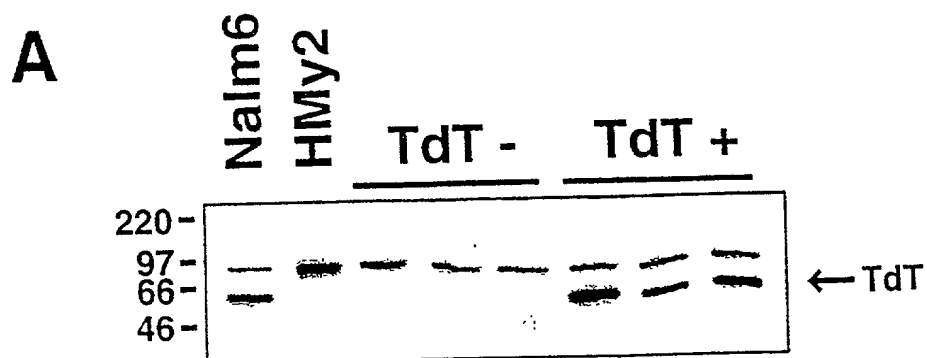


FIG. 5

TdT positive

TdT negative		TdT positive	
Deletion		Deletion	Insertion (+/- Del/Dup)
A62 GGTCTTCAGTGGTACTA		D27 GGAGACCTCACTCGG	D3 CGGCGCAGGACTGTGAAGC
A120 GTGGATTCGGGAA		D31 ACCCTCCTCGG	D56 ATGCTGGG.50bp.LAGSAGGTGGG.50bp.CASGGAGGGG
A276 TATTACCTGTG.18bp.TACTAGGGG		D219 CCTGAATGTCNC	D71 GTGGTTACTACTG
A306 GAGGTAAGGTATG		D150 CACCAATACAC	D75 TTTACTATGGAGTT
B93 CCGCCAAGCCCCA		D109 AAGGGCTGGAGT	D126 TGGGGAATCAATCATAGTGA
B98 AGCCCCAGGAA		E38 CCTCACTCTCGGTGT	D223 AAGTGCACCCGCGCTCTGTG
B227 TGAGCTCTGTGAGCGC		E81 CTGGAGTTGA.37bp.TGAGTGGATT	D232 TCTTTAGAGGCTGCGCCGCTCTGTGAGTGGAGCGGAC
C82 TGGAGTTGA.37bp.GAGTGGATTG		E88 TGGATCCTGCTAGCCCC	D235 GTGAACGAGCGCCGCG
C209 AGCACCCTCTCCCTGAGTTGAGCTC		E93 CCGCAAGCCCCA	D252 GGTCTGTATTACTGTGGAGA
C187 ATATCAATGACAGCTCCAGAGCACC		E136 AATCAATGTTGAGGACCACTAAGCCC	D268 GCGAGAATATGATT
U26 CGGAGACCTGTGTC		F66 CTTCAGTGGTTACTACTGGAGTT	D275 TTTATTAAGTAGGGC
U199 AGTCCAAAGAGCAG		F183 ATCAGTAACAGGT	D332 AAGGGAAGCAG
U208 AAGCAGCTGTCTC		F215 TCTCCCTGA.18bp.CGCCGGGAC	E3 GGGCGCAGGA.51bp.CTTCACTGGT
U268 GCGAGAATTATTACTAGGG		F267 TCGAGAGTTATTA	E51 TGTTTATGGT.15bp.TACTACTGGAG
Duplication		Duplication	
A255 TGTGAGAGGTTATTCAGAGTTATTTAGGG		D55 TATGTTGG.41bp.AGGGTTGG.41bp.AGGGTAAGG	E80 ACTGGAAGCTTGGAT
A113 GGCTGGAGTGGATTGGG.52bp.T		D123 GATTGGGAAATCAATCATAGTGGAGCGGAA	E263 ACTGTGCGAGGTTTACTAGGGCG
			F89 GGTATCCGCCAGGCCCCAGGGAGGGG
			F168 CTCAAAGTCAAT
			F195 AGACACCTCCAAAGAGCACCTC
			F199 AGTCCAGAAAGACCTTGA
			F242 CTGCGGACACGCGCTGTATTACTGTGGAGA
			F260 ATTACTGTGAAGAG
			F264 CTGTGCGAGAG.48bp.CGTCTGGGGC
Events with flanking single nucleotide substitutions		Events with flanking single nucleotide substitutions	
Deletion		Deletion	
B123 GATTGGGAATC		D45 CTGCGGCTTTATGGTGGGTCTTCA	
C109 AAGGCTGGAGT		D164 CTTCCCTGAGAGTCCA	
		D216 CTCCCTGAG.22bp.CGGAACAGGC	
		E11 GACTGTAGGCC	
		E54 TTTATGGGG.25bp.GTTGATCCG	
		F188 TATCAAGAGACAGCTCCAGAACCT	
		F220 CTGAAGCTGAGCTCTGTGAGGCC	
Duplication		Duplication	
A16 TTTAGCTCTGGAGTAAAGCTTTGGAGA			
U180 AGTCACCAATACAGACCATATCAGTAGACA			

FIG. 6

FIG. 7

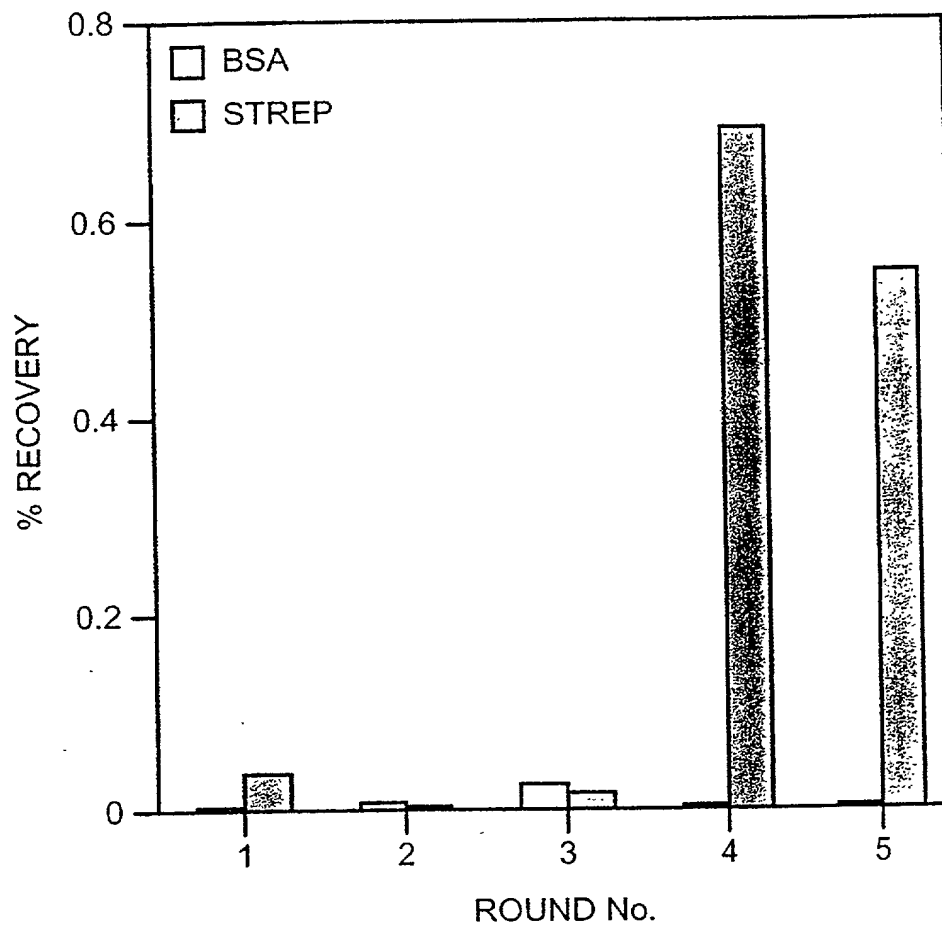


FIG. 8

FIG. 9

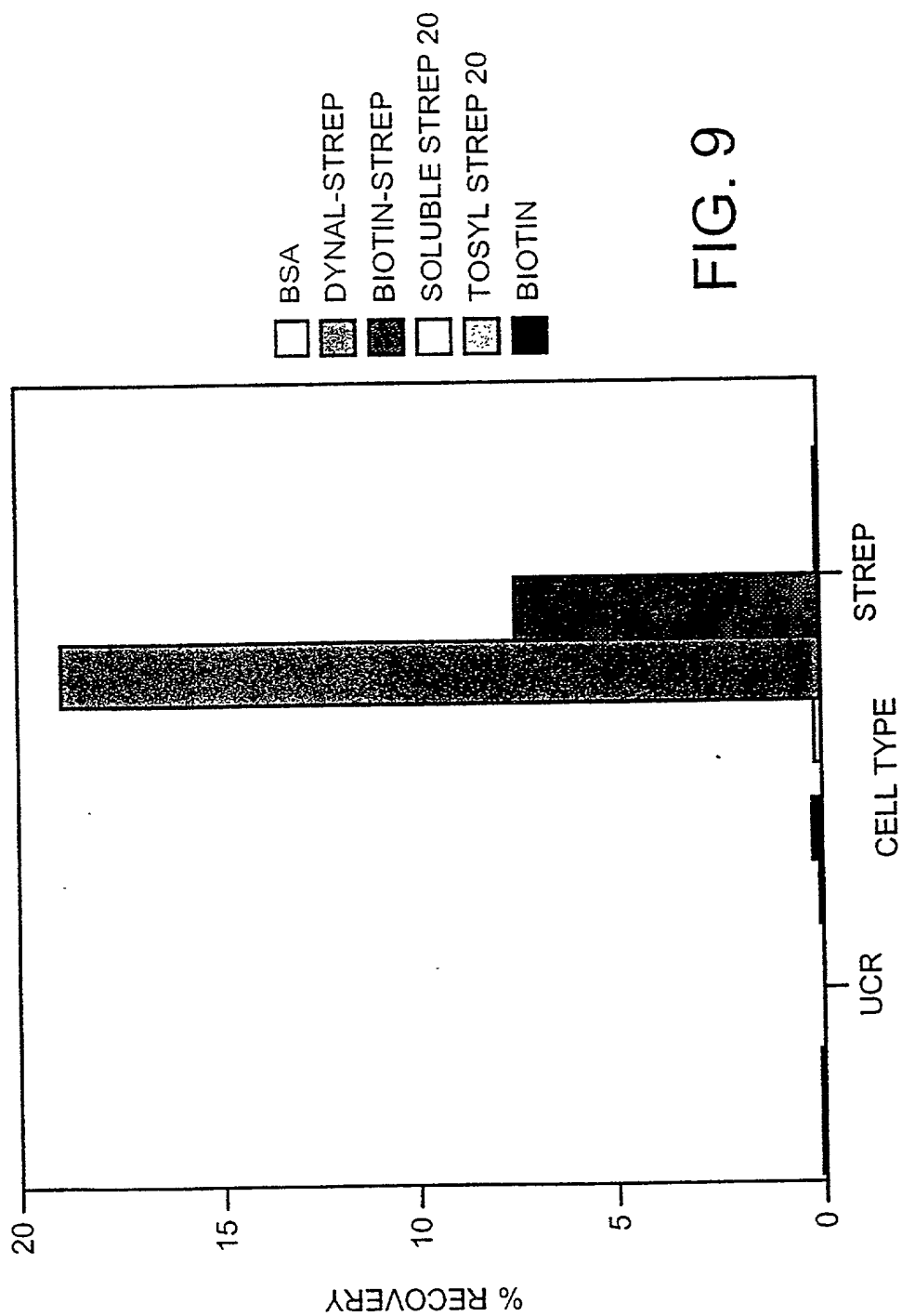


FIG. 9

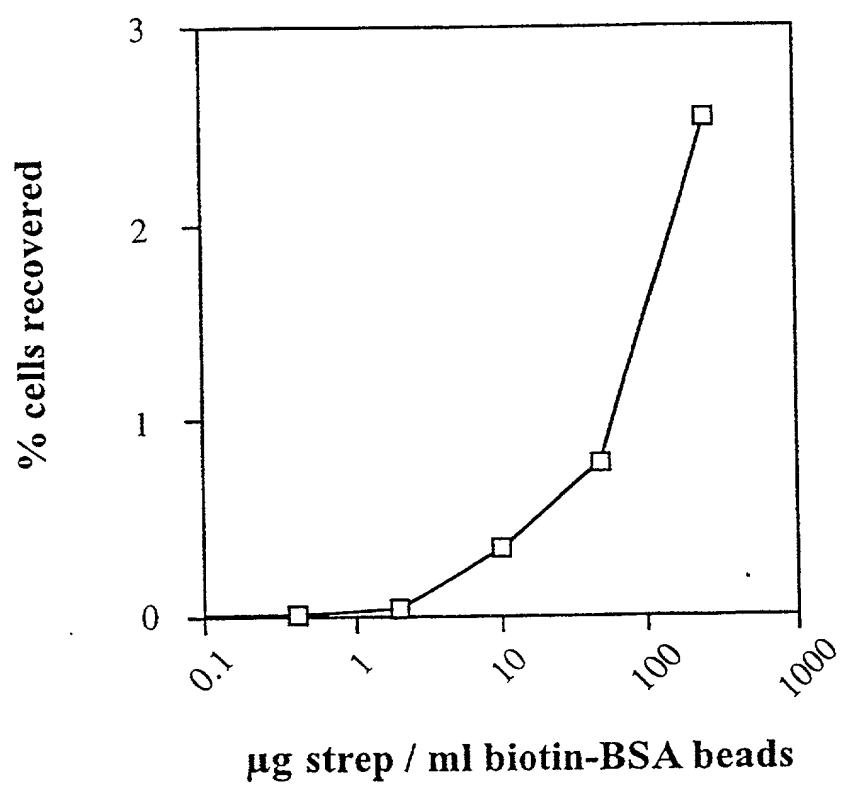


FIG. 10

FIG. 11

VH

1/1
 TGG GGC GCA GGA CTG TTG AAG CCT TCG GAG ACC CTG TCC CTC ACC TGC GGT GTT TAT GGT
 W G A G L L K P S E T L S L T C G V Y G

31/11
 61/21
 GGG TCC TTC AGT GGT TAC TAC TGG AGC TGG ATC CGC CAG CCC CCA GGG AAG GGG CTG GAG
 G S F S G Y Y W S W I R Q P P G K G L E
 GGA
 G AGT
 S
 ATT
 I

91/31
 121/41
 TGG ATT GGG GAA ATC AAT CAT AGT GGA AGC ACC AAC TAC AAC CCG TCC CTC AAG AGT CGA
 W I G E I N H S G S T N Y N P S L K S R

151/51
 181/61
 GTC ACC ATA TCA GTA GAC ACG TCC AAG AAG CAG CTC TCC CTG AAG TTG AGC TCT GTG AAC
 V T I S V D T S K K H L S L K L S S AAC
 CAC
 H

211/71
 241/81
 GCC GCG GAC ACG GCT GTG TAT TAC TGT GCG AGA GTT ATT ACT AGG GCG AGT CCT GGA ACA
 A A D T A V Y Y C A R V I T R A S P G T

271/91
 301/101
 GAC GGG AGG TAC GGT ATG GAC GTC TGG GGC CAA GGG ACC ACG
 D G R Y G M D V W G Q G T T
 AGC
 S

331/111

VL

1/1
 CCT GCC TCC GTG TCT GGG TCT CCT GGA CAG TCG ATC ACC ATC TCC TGC ACT GGA ACC AGC
 P A S V S G S P G Q S I T I S C T G T S
 TAT
 Y

31/11
 61/21
 AGT GAC GTT GGT GAT AAC TAT GTC TCC TGG TAC CAA AAC CCA GGC AAA GCC CCC
 S D V G G Y N Y V S W Y Q Q N P G K A P
 TTT TGT
 F C

91/31
 121/41
 AAA CTC ATG ATT TAT GAT GTC AGT AAT CGG CCC TCA GGG ATT TCT AAT CGC TTC TCT GGC
 K L M I Y D V S N R P S G I S N R F G S
 AAT
 N CGA TTA
 R L

151/51
 181/61
 TCC AAG TCT GGC AAC ACG GCC TCC CTG ACC ATC TCT GGG CTC CAG GCT GAC GAC GAG GCT
 S K S G N T A S L T I S G L Q A D D E A
 ATC
 I

211/71
 241/81
 GAT TAT TAC TGC ACC TCA TAT ATA AAC GAC AGC AAT TCT CAG GTA TTC GGC GGA GGG ACC
 D Y Y C T S Y T N D S N S Q V F G G T
 ACT
 T

271/91

FIG. 11 CONT'D

FIG. 12
IgM in supernatant

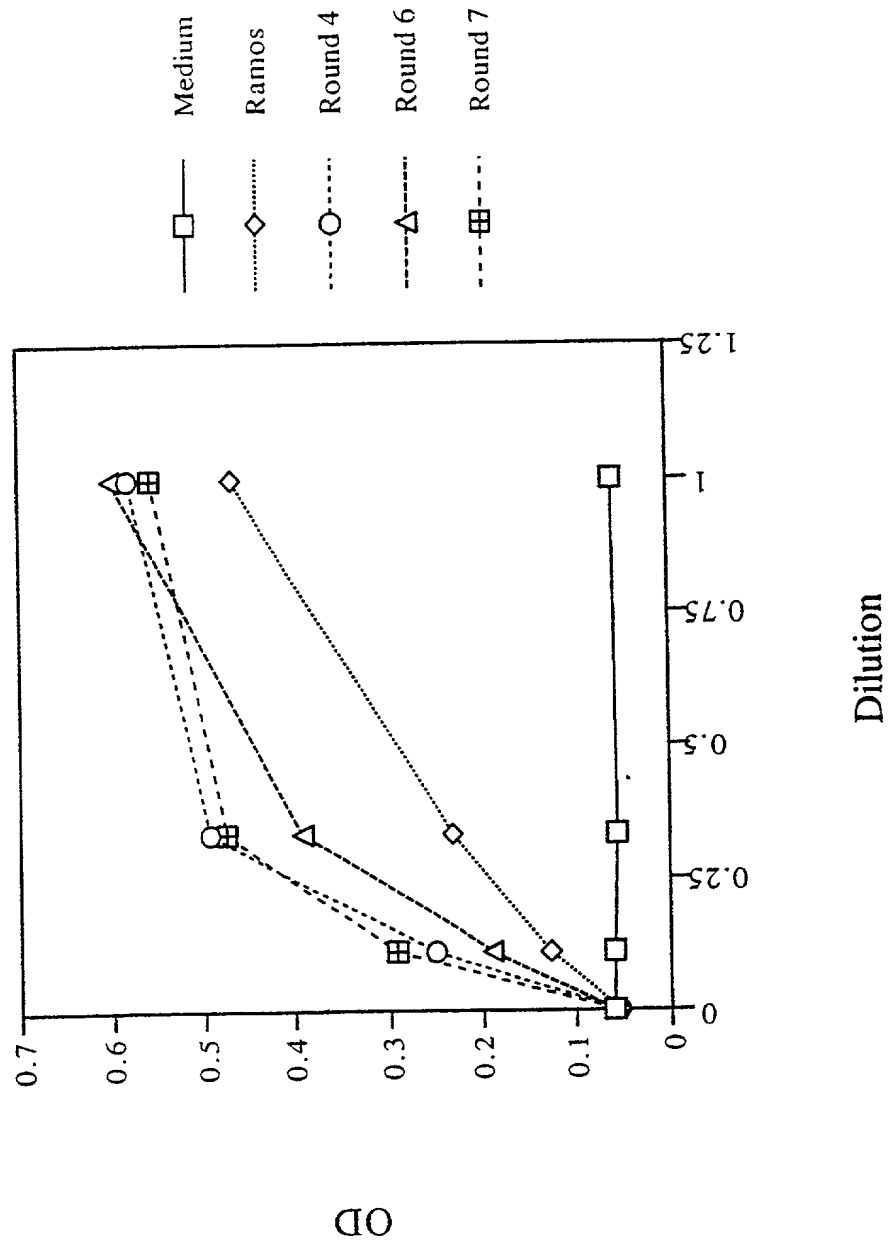


FIG. 13
Streptavidin binding of Supernatants: ELISA

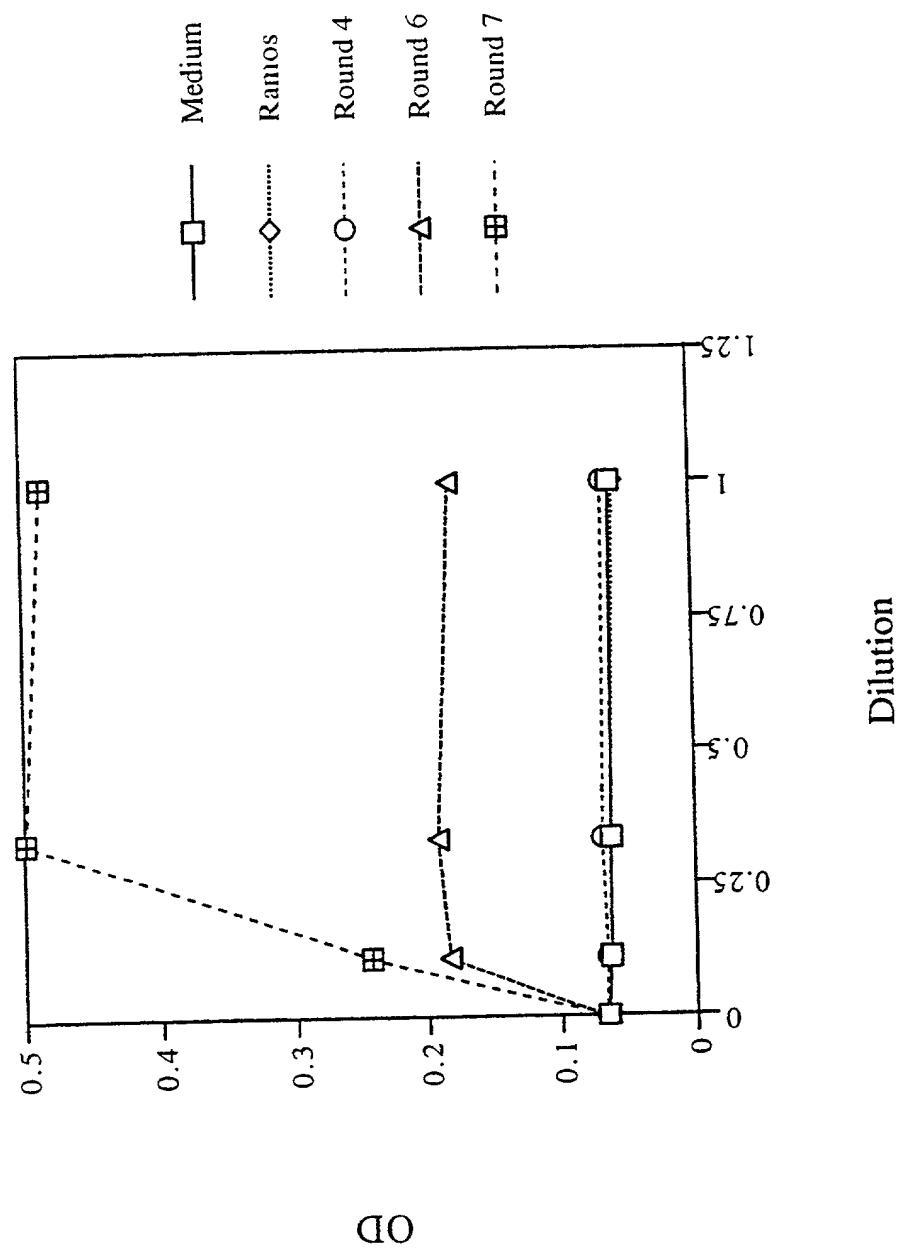
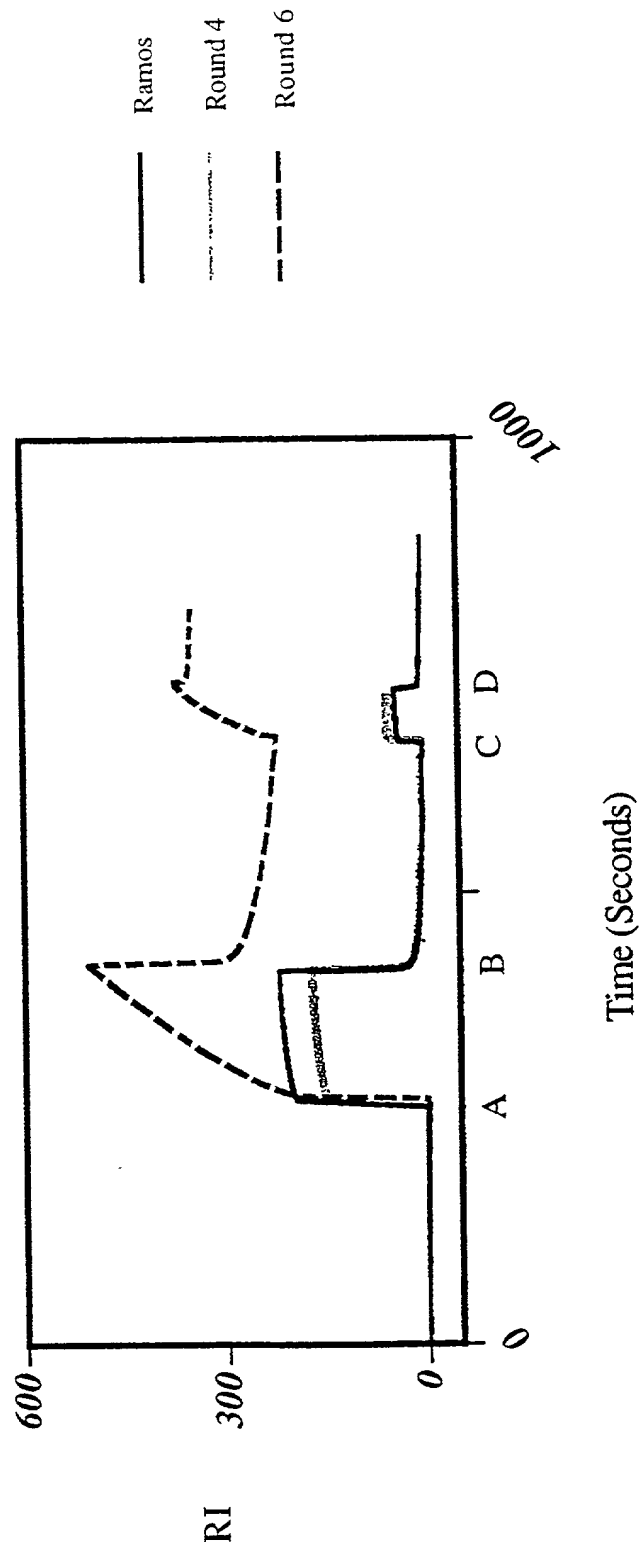
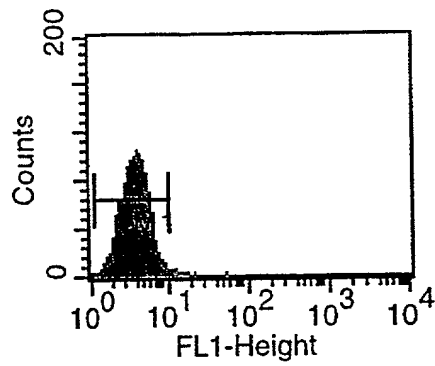


FIG. 14
Streptavidin binding of Supernatants: Biacore

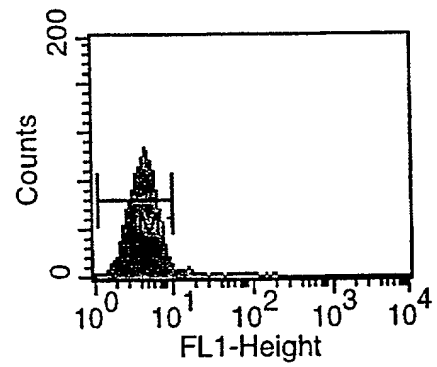


Ramos

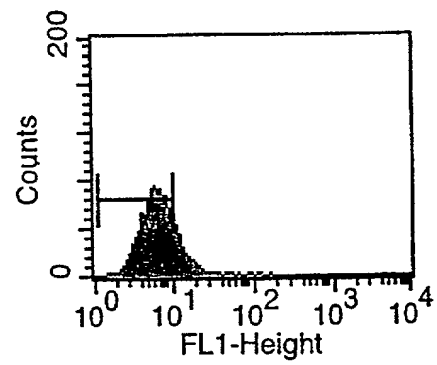
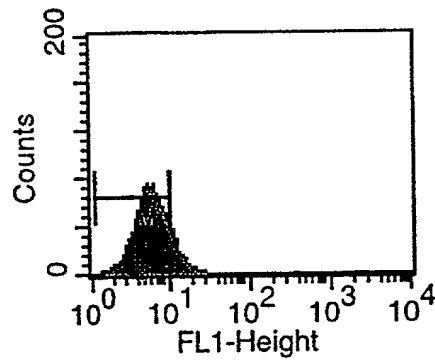
CD8-bio 1/500



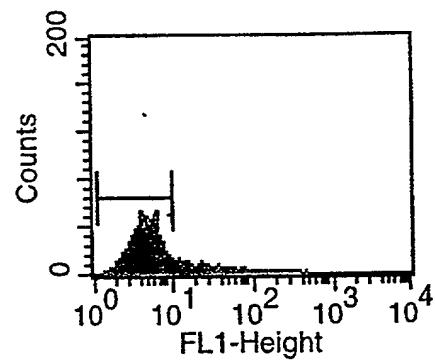
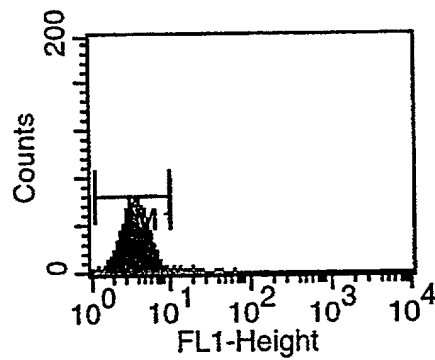
CD8-bio 1/500
Strep-FITC 1/50



Ramos
IgM -ve



Round 4



Round 6

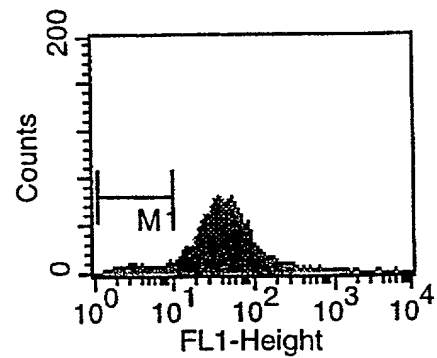
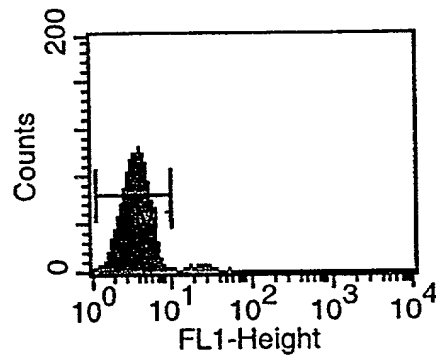


FIG. 15

FIG. 16

VH

1/1 31/11
 TGG GGC GCA GGA CTG TTG AAG CCT TCG GAG ACC CTG TCC CTC ACC TGC GGT GTT TAT GGT
 W G A G L L K P S E T L S L T C G V Y G

 61/21 CDR1 91/31
 GGG TCC TTC AGT GGT TAC TAC TGG AGC TGG ATC CGC CAG CCC CCA GGG AAG GGG CTG GAG
 G S F S G Y Y W S W I R Q P P G K G L E

 121/41 CDR2 151/51
 TGG ATT GGG GAA ATC AAT CAT AGT GGA AGC ACC AAC TAC AAC CCG TCC CTC AAG AGT CGA
 W I G E I N H S G S T N Y N P S L K S R

 181/61 211/71
 GTC ACC ATA TCA GTA GAC ACG TCC AAG AAG CAG CTC TCC CTG AAG TTG AGC TCT GTG AAC
 V T I S V D T S K K H L S L K L S S V N

 241/81 271/91 DJ
 GCC GCG GAC ACG GCT GTG TAT TAC TGT GCG AGA GTT ATT ACT AGG GCG AGT CCT GGA ACA
 A A D T A V Y Y C A R V I T R A S P G T

 301/101 331/111
 GAC GGG AGG TAC GGT ATG GAC GTC TGG GGC CAA GGG ACC ACG
 D G R Y G M D V W G Q G T T
 AGC
 S

VL

1/1
 CCT GCC TCC GTG TCT GGG TCT CCT GGA CAG TCG ATC ACC ATC TCC TGC ACT GGA ACC AGC CDR1
 P A S V S G S P G Q S I T I S C T G T S

31/31
 61/21
AGT GAC GTT GGT GGT TAT AAC TAT GTC TCC TGG TAC CAA AAC CCA GGC AAA GCC CCC
 S D V G G Y N Y V S W Y Q Q N P G K A P
 TTT TGT
 F C

121/41
 CDR2
AAA CTC ATG ATT TAT GAT GTC AGT AAT CGG CCC TCA GGG ATT TCT AAT CGC TTC TCT GGC
 K L M I Y D V S N R P S G I S N R F G S
 GCT
 A

151/51
 181/61
 TCC AAG TCT GGC AAC ACG GCC TCC CTG ACC ATC TCT GGG CTC CAG GCT GAC GAC GAG GCT
 S K S G N T A S L T I S G L Q A D D E A

211/71
 241/81
 CDR3
GAT TAT TAC TGC ACC TCA TAT ACA AAC GAC AGC AAT TCT CAG GTA TTC GGC GGA GGG ACC
 D Y Y C T S Y T N D S N S Q V F G G T

271/91

FIG. 16CONT'D

In Vitro Maturation

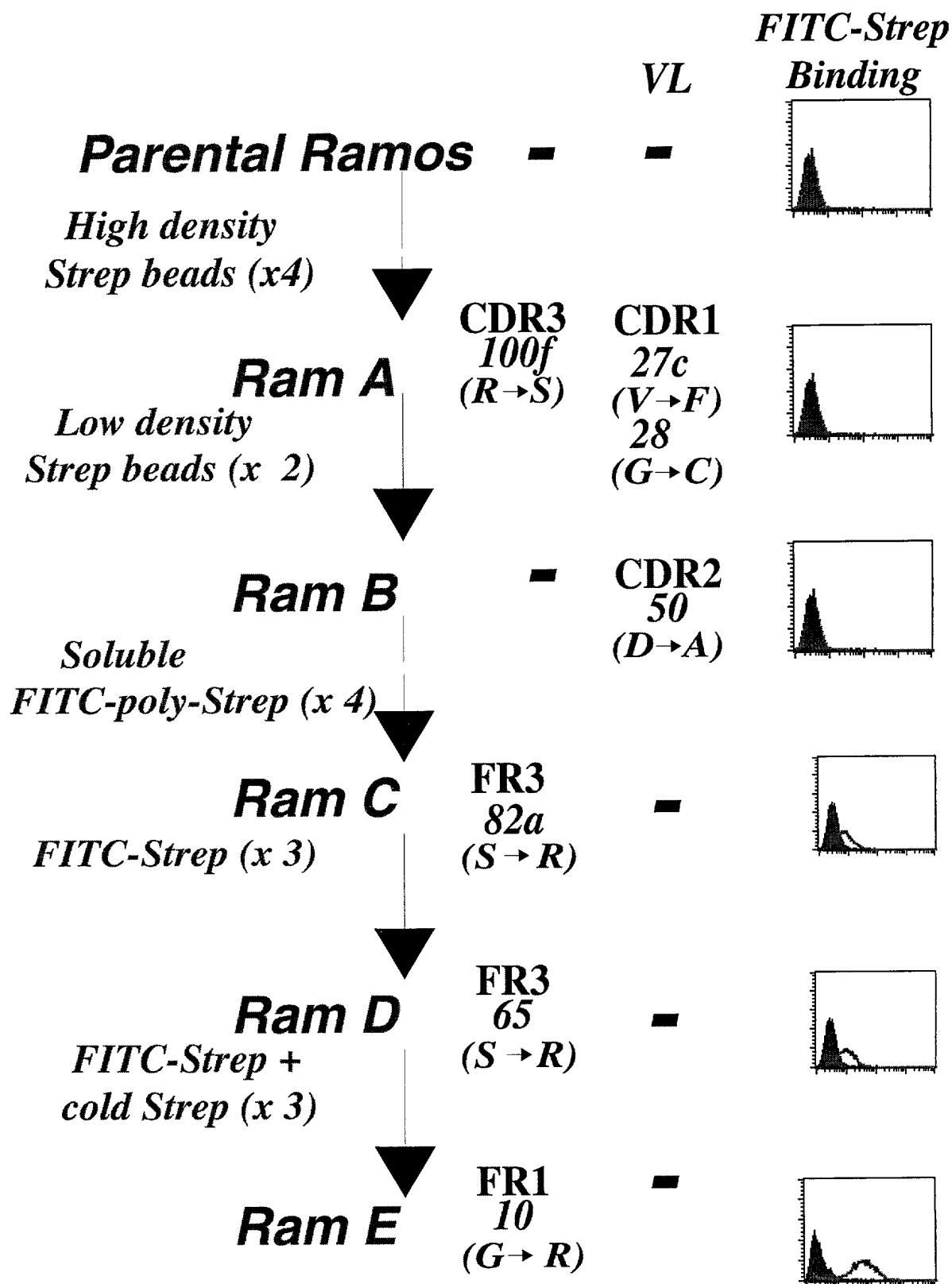
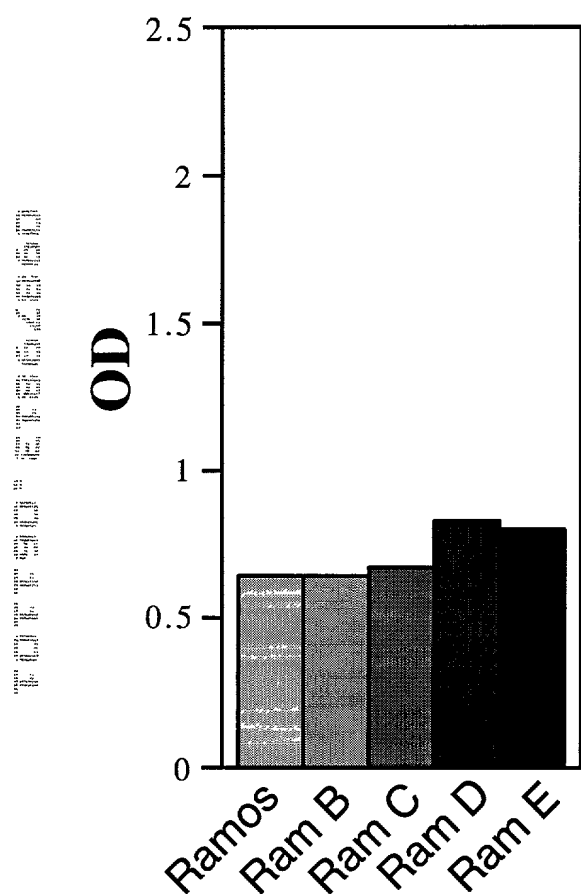


FIGURE 17

IgM ELISA



Strep ELISA

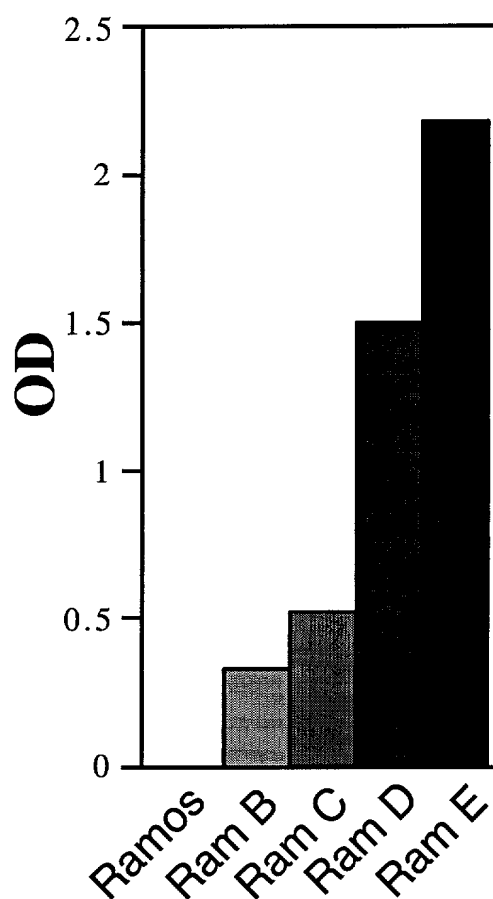
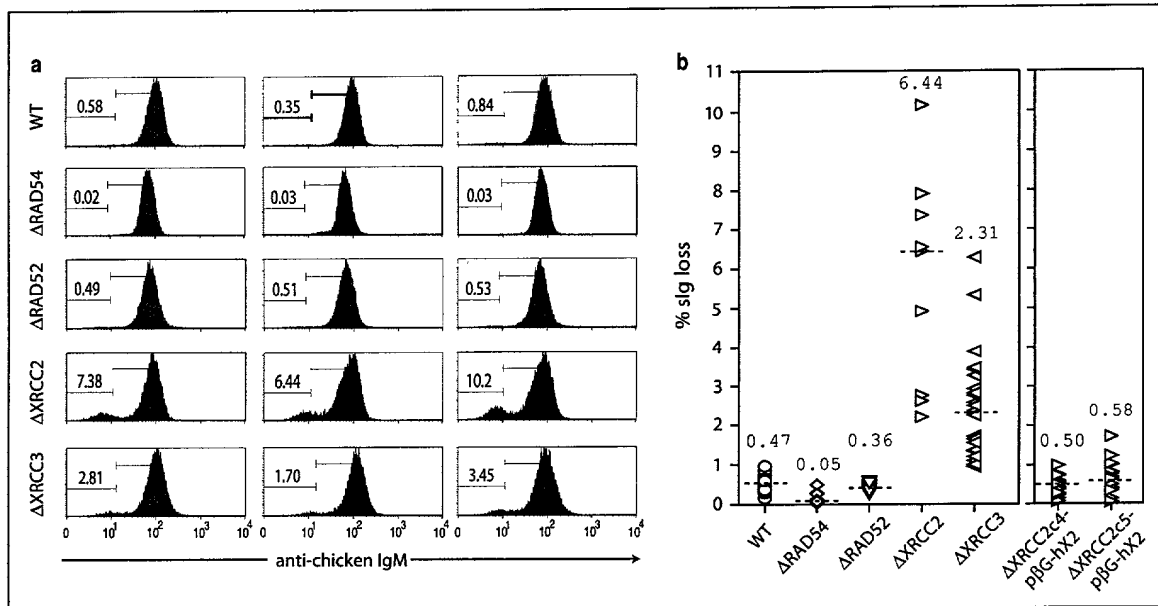
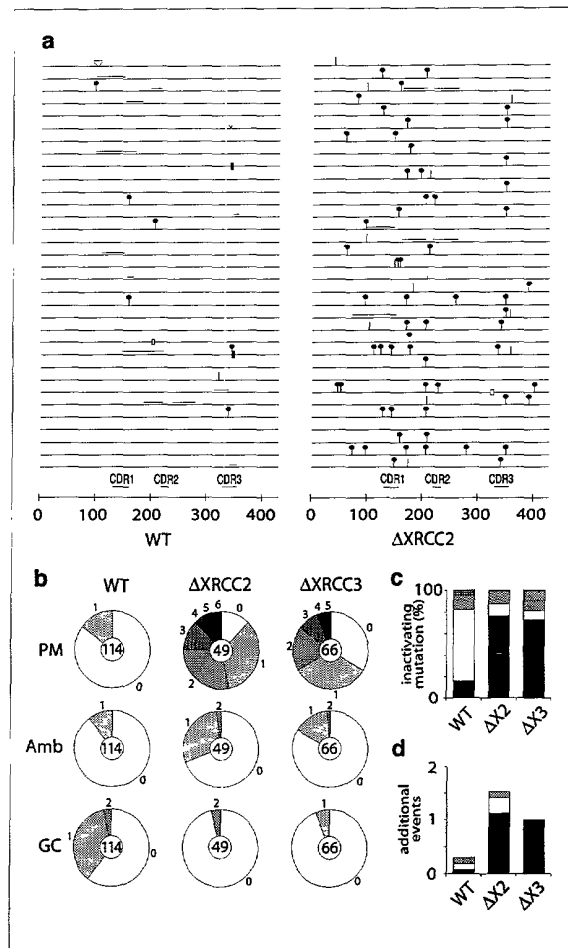


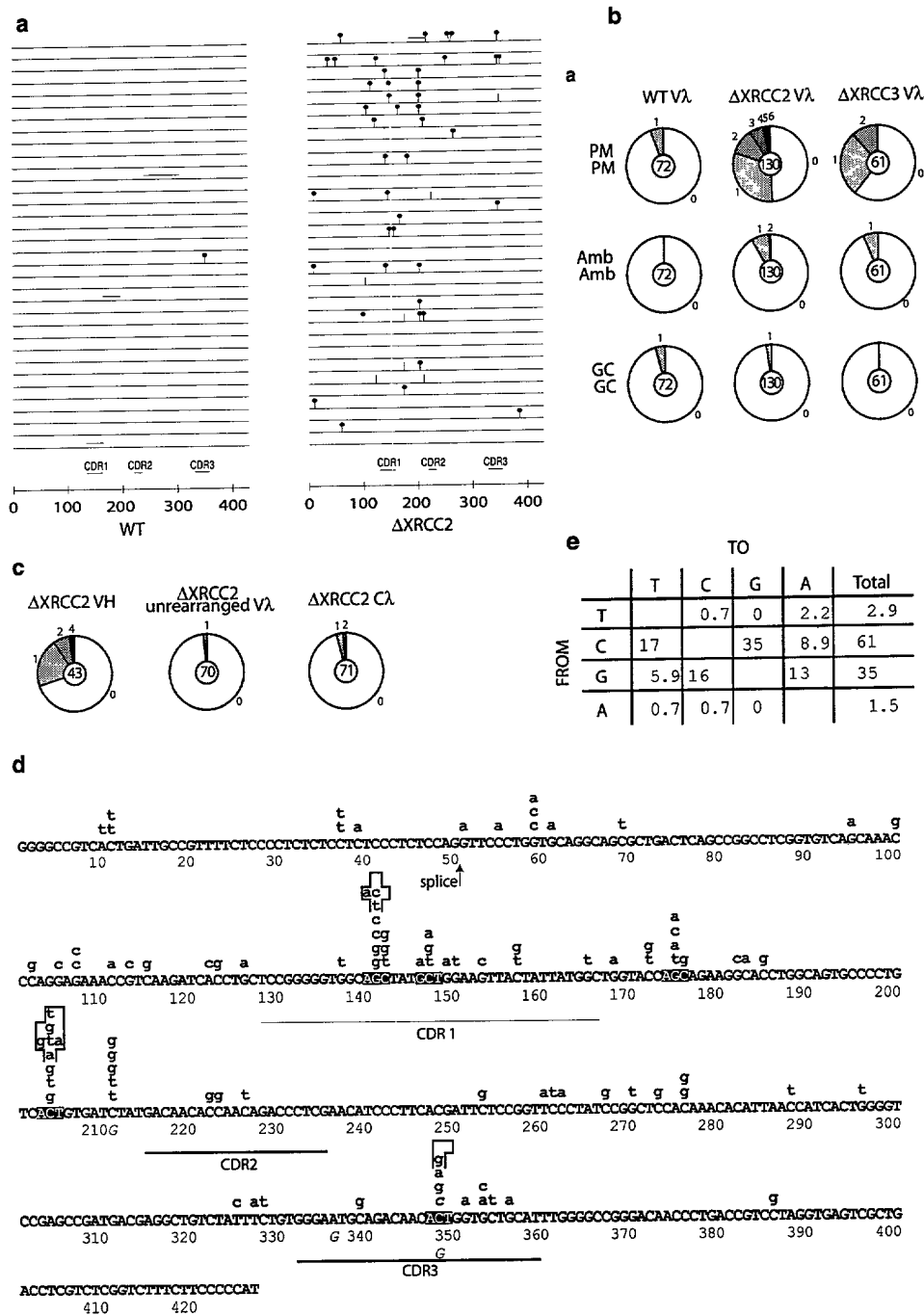
FIGURE 18



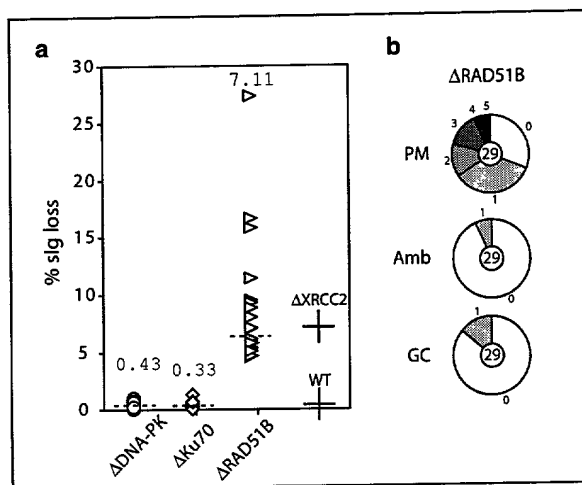
FIGURES 19A-B



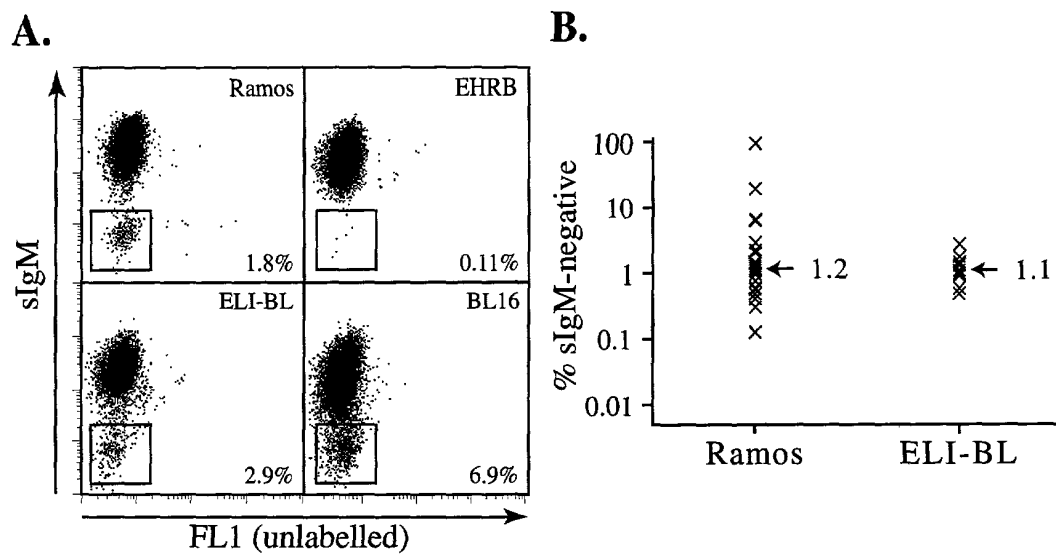
FIGURES 20A-C



FIGURES 21A-D



FIGURES 22A-B



C.

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GTG CAG CTG GTG GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG GGG TCC CTG AGA CTC TCA TGT GCA
V  Q  L  V  E  S  G  G  G  V  V  Q  P  G  G  S  L  R  L  S  C  A
1

GCC TCT GGA TTC ACC GTC AGT AGC AAC TAC ATG ACC TGG GTC CGC CAG GCT CCA GGG AAG GGG CTG
A  S  G  F  T  V  S  S  N  Y  M  T  W  V  R  Q  A  P  G  K  G  L
30

GAG TGG GTG TCA CTT ATT TAT AGC GGT GGT AGC ACA ACA TAT TAC GCA GAG TCC GTG AAG GGC CGA
E  W  V  S  L  I  Y  S  G  G  S  T  T  Y  Y  A  E  S  V  K  G  R
50

TTC ACC ATC TCC AGA GAC AAT TCC AAA AAC ACG ATG TAT CTT CAA ATG AAC AGC CTG AGA GTA GAG
F  T  I  S  R  D  N  S  K  N  T  L  Q  M  N  S  L  R  V  E  D  T
70

GAC ACG GCT GTG TAT TAC TGT GCG GGA GAC CTG AAC AGC ACC TCG GTA GGG ACT AAT AAT TTC TAC
M  N  S  V  R  V  E  D  T  A  V  N  S  T  S  V  G  T  N  N  F  Y
90

ATG GAC GTC TGG GGC AAA GGG ACC ACG GTC ACC GTC TCC TCA
M  D  V  W  G  K  G  T  T  V  T  V  S  S
120
  
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FIGURES 23A-C